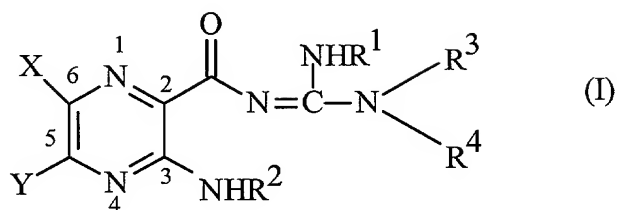


# CLAIMS:

1. A compound represented by formula (I):



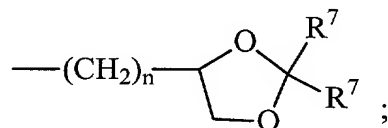
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

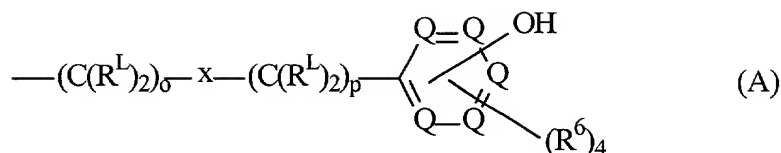
Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or  $-N(R^2)_2$ ;

$R^1$  is hydrogen or lower alkyl;

each  $R^2$  is, independently,  $-R^7$ ,  $-(CH_2)_m-OR^8$ ,  $-(CH_2)_m-NR^7R^{10}$ ,  $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-(CH_2CH_2O)_m-R^8$ ,  $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  $-(CH_2)_n-C(=O)NR^7R^{10}$ ,  $-(CH_2)_n-Z_g-R^7$ ,  $-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-(CH_2)_n-CO_2R^7$ , or

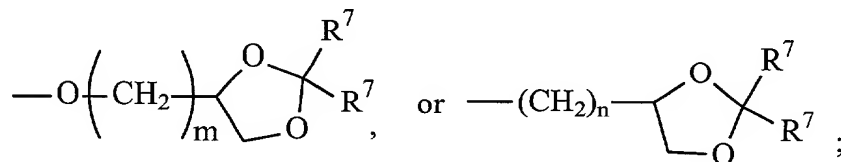


$R^3$  and  $R^4$  are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of  $R^3$  and  $R^4$  is a group represented by formula (A):



wherein

each  $R^L$  is, independently,  $-R^7$ ,  $-(CH_2)_n-OR^8$ ,  $-O-(CH_2)_m-OR^8$ ,  
 $-(CH_2)_n-NR^7R^{10}$ ,  $-O-(CH_2)_m-NR^7R^{10}$ ,  $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  
 $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-(CH_2CH_2O)_m-R^8$ ,  
 $-O-(CH_2CH_2O)_m-R^8$ ,  $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  
 $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  $-(CH_2)_n-C(=O)NR^7R^{10}$ ,  
 $-O-(CH_2)_m-C(=O)NR^7R^{10}$ ,  $-(CH_2)_n-(Z)_g-R^7$ ,  $-O-(CH_2)_m-(Z)_g-R^7$ ,  
 $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  
 $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  
 $-(CH_2)_n-CO_2R^7$ ,  $-O-(CH_2)_m-CO_2R^7$ ,  $-OSO_3H$ ,  $-O$ -glucuronide,  $-O$ -glucose, or



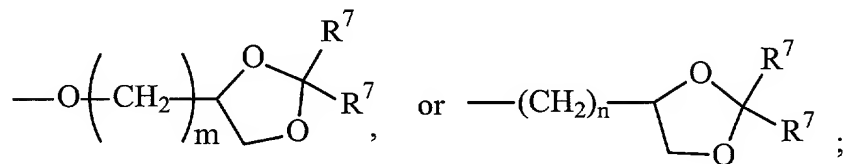
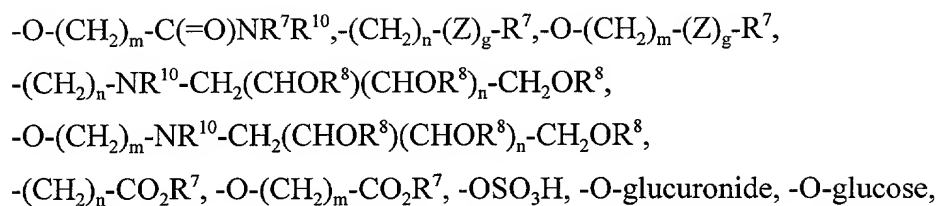
each  $x$  is, independently,  $O$ ,  $NR^7$ ,  $C=O$ ,  $CHOH$ ,  $C=N-R^6$ , or represents a single bond;

each  $o$  is, independently, an integer from 0 to 10;

each  $p$  is, independently, an integer from 0 to 10;

with the proviso that (a) the sum of  $o$  and  $p$  in each contiguous chain is from 1 to 10 when  $x$  is  $O$ ,  $NR^7$ ,  $C=O$ , or  $C=N-R^6$  or (b) that the sum of  $o$  and  $p$  in each contiguous chain is from 4 to 10 when  $x$  represents a single bond;

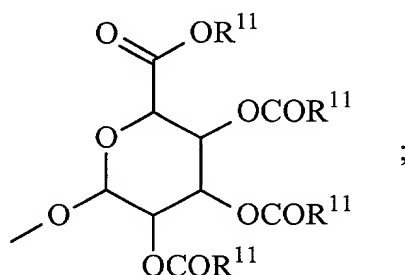
each  $R^6$  is, independently,  $-R^7$ ,  $-OH$ ,  $-OR^{11}$ ,  $-N(R^7)_2$ ,  $-(CH_2)_m-OR^8$ ,  
 $-O-(CH_2)_m-OR^8$ ,  $-(CH_2)_n-NR^7R^{10}$ ,  $-O-(CH_2)_m-NR^7R^{10}$ ,  
 $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  
 $-(CH_2CH_2O)_m-R^8$ ,  $-O-(CH_2CH_2O)_m-R^8$ ,  $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  
 $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  $-(CH_2)_n-C(=O)NR^7R^{10}$ ,



wherein when two  $R^6$  are  $-OR^{11}$  and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two  $R^6$  may be bonded together to form a methylenedioxy group;

each  $R^7$  is, independently, hydrogen or lower alkyl;

each  $R^8$  is, independently, hydrogen, lower alkyl,  $-C(=O)-R^{11}$ , glucuronide, 2-tetrahydropyranyl, or



each  $R^9$  is, independently,  $-CO_2R^7$ ,  $-CON(R^7)_2$ ,  $-SO_2CH_3$ , or  $-C(=O)R^7$ ;

each  $R^{10}$  is, independently,  $-H$ ,  $-SO_2CH_3$ ,  $-CO_2R^7$ ,  $-C(=O)NR^7R^9$ ,  $-C(=O)R^7$ , or  $-CH_2-(CHOH)_n-CH_2OH$ ;

each  $Z$  is, independently,  $CHOH$ ,  $C(=O)$ ,  $CHNR^7R^{10}$ ,  $C=NR^{10}$ , or  $NR^{10}$ ;

each  $R^{11}$  is, independently, lower alkyl;

each  $g$  is, independently, an integer from 1 to 6;

each  $m$  is, independently, an integer from 1 to 7;

each  $n$  is, independently, an integer from 0 to 7;

each  $Q$  is, independently,  $C-R^5$ ,  $C-R^6$ , or a nitrogen atom, wherein at most three  $Q$  in a ring are nitrogen atoms;

or a pharmaceutically acceptable salt thereof, and  
inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

2. The compound of Claim 1, wherein Y is  $-NH_2$ .

5 3. The compound of Claim 2, wherein  $R^2$  is hydrogen.

4. The compound of Claim 3, wherein  $R^1$  is hydrogen.

5. The compound of Claim 4, wherein X is chlorine.

6. The compound of Claim 5, wherein  $R^3$  is hydrogen.

7. The compound of Claim 6, wherein each  $R^L$  is hydrogen.

10 8. The compound of Claim 7, wherein o is 4.

9. The compound of Claim 8, wherein p is 0.

10. The compound of Claim 9, wherein x represents a single bond.

11. The compound of Claim 10, wherein each  $R^6$  is hydrogen.

12. The compound of Claim 11, wherein at most one Q is a nitrogen atom.

15 13. The compound of Claim 12, wherein no Q is a nitrogen atom.

14. The compound of Claim 1, wherein

X is halogen;

Y is  $-N(R^7)_2$ ;

$R^1$  is hydrogen or  $C_1$ - $C_3$  alkyl; and

20  $R^2$  is  $-R^7$ ,  $-(CH_2)_m-OR^7$ , or  $-(CH_2)_n-CO_2R^7$ ;

R<sup>3</sup> is a group represented by formula (A); and

R<sup>4</sup> is hydrogen, a group represented by formula (A), or lower alkyl;

15. The compound of Claim 14, wherein

X is chloro or bromo;

Y is -N(R<sup>7</sup>)<sub>2</sub>;

R<sup>2</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

at most three R<sup>6</sup> are other than hydrogen as defined above;

at most three R<sup>L</sup> are other than hydrogen as defined above; and

at most 2 Q are nitrogen atoms.

16. The compound of Claim 15, wherein Y is -NH<sub>2</sub>.

17. The compound of Claim 16, wherein

R<sup>4</sup> is hydrogen;

at most one R<sup>L</sup> is other than hydrogen as defined above;

at most two R<sup>6</sup> are other than hydrogen as defined above; and

at most 1 Q is a nitrogen atom.

18. The compound of Claim 17, wherein x is O, NR<sup>7</sup>, C=O, CHOH, or C=N-R<sup>6</sup>.

19. The compound of Claim 17, wherein x represents a single bond.

20. The compound of Claim 1, wherein x is O, NR<sup>7</sup>, C=O, CHOH, or C=N-R<sup>6</sup>.

21. The compound of Claim 1, wherein x represents a single bond.

22. The compound of Claim 1, wherein each R<sup>6</sup> is hydrogen.

23. The compound of Claim 1, wherein at most two R<sup>6</sup> are other than hydrogen as defined in Claim 1.

24. The compound of Claim 1, wherein one R<sup>6</sup> is other than hydrogen as defined in Claim 1.

25. The compound of Claim 1, wherein one R<sup>6</sup> is -OH.

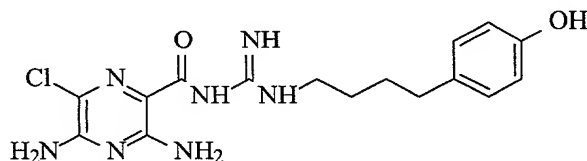
26. The compound of Claim 1, wherein each R<sup>L</sup> is hydrogen.

27. The compound of Claim 1, wherein at most two R<sup>L</sup> are other than hydrogen as defined in Claim 1.

28. The compound of Claim 1, wherein one R<sup>L</sup> is other than hydrogen as defined in Claim 1.

29. The compound of Claim 1, wherein x represents a single bond and the sum of o and p is 4 to 6.

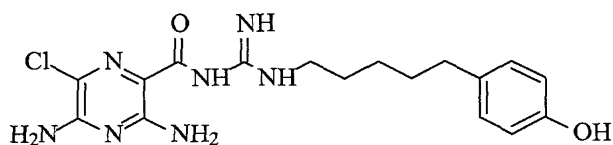
30. The compound of Claim 1, which is represented by the formula



31. The compound of Claim 30, which is in the form of a pharmaceutically acceptable salt.

32. The compound of Claim 31, which is in the form of a hydrochloride salt.

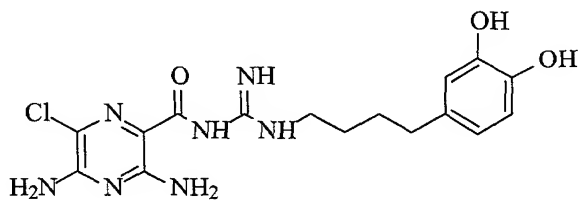
33. The compound of Claim 1, which is represented by the formula



34. The compound of Claim 33, which is in the form of a pharmaceutically acceptable salt.

35. The compound of Claim 34, which is in the form of a hydrochloride salt.

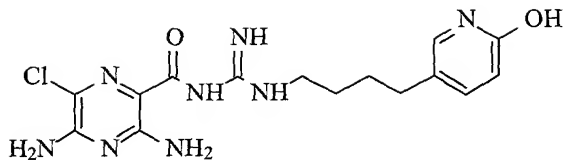
36. The compound of Claim 1, which is represented by the formula



37. The compound of Claim 36, which is in the form of a pharmaceutically acceptable salt.

38. The compound of Claim 37, which is in the form of a hydrochloride salt.

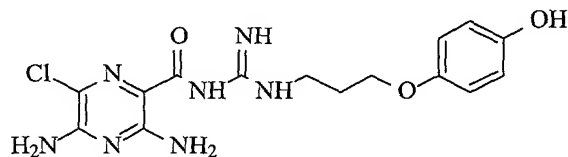
39. The compound of Claim 1, which is represented by the formula



40. The compound of Claim 39, which is in the form of a pharmaceutically acceptable salt.

41. The compound of Claim 40, which is in the form of a hydrochloride salt.

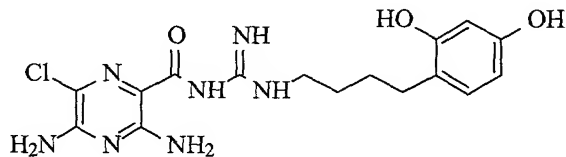
42. The compound of Claim 1, which is represented by the formula



43. The compound of Claim 42, which is in the form of a pharmaceutically acceptable salt.

44. The compound of Claim 43, which is in the form of a hydrochloride salt.

45. The compound of Claim 1, which is represented by the formula





46. The compound of Claim 45, which is in the form of a pharmaceutically acceptable salt.

47. The compound of Claim 46, which is in the form of a hydrochloride salt.

48. The compound of Claim 1, which is in the form of a pharmaceutically acceptable salt.

49. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

50. A method of promoting hydration of mucosal surfaces, comprising:  
administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

51. A method of restoring mucosal defense, comprising:  
topically administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject in need thereof.

52. A method of blocking sodium channels, comprising:  
contacting sodium channels with an effective amount of the compound of Claim 1.

53. A method of treating chronic bronchitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

54. A method of treating cystic fibrosis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

55. A method of treating sinusitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

5 56. A method of treating vaginal dryness, comprising:  
administering an effective amount of the compound of Claim 1 to the vaginal tract of a subject in need thereof.

57. A method of treating dry eye, comprising:  
administering an effective amount of the compound of Claim 1 to the eye of a subject in need thereof.

10 58. A method of promoting ocular hydration, comprising:  
administering an effective amount of the compound of Claim 1 to the eye of a subject.

59. A method of promoting corneal hydration, comprising:  
administering an effective amount of the compound of Claim 1 to the eye of a subject.

15 60. A method of promoting mucus clearance in mucosal surfaces, comprising:  
administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

61. A method of treating Sjogren's disease, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

20 62. A method of treating distal intestinal obstruction syndrome, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

63. A method of treating dry skin, comprising:  
administering an effective amount of the compound of Claim 1 to the skin of a subject  
in need thereof.

5 64. A method of treating esophagitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.

65. A method of treating dry mouth (xerostomia), comprising:  
administering an effective amount of the compound of Claim 1 to the mouth of a  
subject in need thereof.

10 66. A method of treating nasal dehydration, comprising:  
administering an effective amount of the compound of Claim 1 to the nasal passages  
of a subject in need thereof.

67. The method of Claim 66, wherein the nasal dehydration is brought on by  
administering dry oxygen to the subject.

15 68. A method of preventing ventilator-induced pneumonia , comprising:  
administering an effective amount of the compound of Claim 1 to a subject on a  
ventilator.

20 69. A method of treating asthma, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.

70. A method of treating primary ciliary dyskinesia, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.

71. A method of treating otitis media, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

5 72. A method of inducing sputum for diagnostic purposes, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

10 73. A method of treating chronic obstructive pulmonary disease, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

15 74. A method of treating emphysema, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

20 75. A method of treating pneumonia, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

76. A method of treating constipation, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

20 77. The method of Claim 76, wherein the compound is administered orally or via a suppository or enema.

78. A method of treating chronic diverticulitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

79. The present invention also provides a method of treating rhinosinusitis, comprising:

administering an effective amount of the compound of Claim 1 to a subject in need thereof.

5 80. A composition, comprising:  
the compound of Claim 1; and  
a P2Y2 inhibitor.

81. A composition, comprising:  
the compound of Claim 1; and  
a bronchodilator.